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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,417	01/17/2002	David Harrow Gelfand	022101-000320US	4095

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EXAMINER

SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
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1634

MAIL DATE	DELIVERY MODE
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04/25/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/052,417

Applicant(s)

GELFAND ET AL.

Examiner

Jehanne S. Sitton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period **will** apply and **will** expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply **will**, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-8, 11-13, 16, 17, 21-23, 26, 31-35, 39-41, 45, 46, 50, 51 and 82-99 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-8, 11-13, 16-17, 21-23, 26, 31-35, 39-41, 45-46, 50-51, 82-99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Currently, claims 1-3, 6-8, 11-13, 16-17, 21-23, 26, 31-35, 39-41, 45-46, 50-51 and newly added claims 82-99 are pending in the instant application. The amendments and arguments have been thoroughly reviewed but are insufficient to place the instant application in condition for allowance. The following rejections are either reiterated or newly applied as necessitated by amendment. This action is Non-FINAL.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The rejections made under 103 made in the previous office action are withdrawn in view of the newly applied rejections set forth below, as necessitated by amendments.
4. The rejection under 35 USC 112/first paragraph in the previous office action is withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 103

5. Claims 1-3, 6-8, 11-13, 16-17, 21-23, 26, 31, 33-35, 39-41, 45-46, 82-89, and 92-97 are rejected under 35 USC 103(a) as being unpatentable over Brandis I (Brandis et al; US Patent 6,265,193) in view of Baker (Baker et al; US Patent 5,571,706) as evidenced by Cormier (Cormier et al; US Patent 5,418,155).

Brandis I teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-13, col. 6, lines 4-39, col. 8, Tables 1 and 2 at cols 17-22).

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With regard to claims 1-3, 6-8, 33-35, 39-41, and 45-46, Brandis I teaches making the specific mutants in *Taq* polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15, Brandis I teaches making a number of mutants at position 681 of *Taq*, which have at least 3 fold lower discrimination (table 2, cols 21-22). Brandis I teaches kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye (claims 6-9), fluorescein type dyes (col. 4), and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator) (col. 4, lines 35-39). Brandis I teaches that sequence homology between DNA polymerases permits corresponding positions to be assigned to amino acid residues for DNA polymerases other than *Taq*.

With regard to claims 11-13 and 16-17, Brandis I teaches providing polynucleotides encoding the mutant polymerases (abstract, all of col. 11, especially lines 40-45).

With regard to claims 21-23, 26-27, and 31 Brandis I teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

With regard to the various independent claims and dependent which recite that the amino acid at position 4 (exemplified by position 681 in *Taq* by Brandis I) is Arg (R) or Gln (Q), Brandis I does not teach actually making or testing these particular mutants, but does list the amino acids in Table 2, columns 21 and 22. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein" (see col 10, lines 4-10). As evidenced by Cormier, standard conservative groups of amino acids include uncharged polar amino acid group which contains G, S, T, C N, Q and the basic amino acid group which contains K, R, and H.

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Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the particular R and Q mutants in the thermostable polymerase of Brandis I and to have used such mutants as taught by Brandis I in view of the teachings of Brandis I and Baker. Brandis I specifically teaches that the basic amino acid K and H possessed reduced discrimination as did the polar uncharged amino acids S, C, N, T and that most of the mutants have 3 fold lower discrimination. Although Brandis I does not teach having made the mutants, Brandis I does provide motivation to make them as they are specifically enumerated in the disclosure of Brandis I. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein". The ordinary artisan would have had a reasonable expectation of success that the particular R and Q mutants would have possessed reduced discrimination given that 16 of 19 possible amino acid mutants made by Brandis I possessed this property and that other amino acids in the same group as Q and R, respectively, possessed this property in view of the teachings of Baker. The ordinary artisan would have been motivated to make the additional amino acid mutants Q and R taught by Brandis I for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis I. Not only would have been "obvious to try" to make and use the claimed mutants as Brandis I provides specific teaching and motivation to make such mutations in thermostable polymerases, but the prior art of both Brandis I and Baker provide for a reasonable expectation of success. The results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining

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Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

6. Claims 1-3, 6-8, 11-13, 16-17, 21-23, 26, 31, 33-35, 39-41, 45-46, 82-89, and 92-97, are rejected under 35 USC 103(a) as being unpatentable over Brandis II (Brandis et al; US PreGrant Publication 2002/0164591) or Brandis III (Brandis et al; US PreGrant Publication 2006/0088879), each in view of Baker as evidenced by Cormier.

Brandis II and III each teaches and claims mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled nucleotide as compared to a naturally occurring DNA polymerase (see claims 1-8, 15, Tables 1 and 2).

With regard to claims 1-3, 6-8, 33-35, 39-41, and 45-46, Brandis II and III each teaches making the specific mutants in Taq polymerase, which comprises SEQ ID NOS 1-3, as acknowledged by the instant specification at page 15. Brandis II and III each teaches making a number of mutants at position 681 of Taq, which have at least 3 fold lower discrimination (table 2.). Brandis II and III each teaches kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye, fluorescein type dyes, and nucleotides which are any naturally occurring nucleotides or analogs such as 2',3' dideoxynucleotides (chain terminator). Brandis II and III teach that sequence homology between DNA polymerases permits corresponding positions to be assigned to amino acid residues for DNA polymerases other than Taq.

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With regard to claims 11-13 and 16-17, Brandis II and III each teaches providing polynucleotides encoding the mutant polymerases (abstract, claim 9 of Brandis II)

With regard to claims 21-23, 26-27, and 31 Brandis II teaches to use the mutant polymerases in methods of Sanger sequencing such as dideoxy nucleotide chain termination, PCR, polynucleotide labeling, and minisequencing.

With regard to the various independent claims and dependent which recite that the amino acid at position 4 (exemplified by position 681 in Taq by Brandis II and III) is Arg (R) or Gln (Q), Brandis II and II do not teach actually making or testing these particular mutants, but do list the amino acids in Table 2. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein" (see col 10, lines 4-10). As evidenced by Cormier, standard conservative groups of amino acids include uncharged polar amino acid group which contains G, S, T, C N, Q and the basic amino acid group which contains K, R, and H. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the particular R and Q mutants in the thermostable polymerase of Brandis II or III and to have used such mutants as taught by Brandis II or III in view of the teachings of Brandis II or III and Baker. Brandis II and III specifically teach that the basic amino acid K and H possessed reduced discrimination as did the polar uncharged amino acids S, C, N, T and that most of the mutants have 3 fold lower discrimination. Although Brandis II or III do not teach having made the mutants, Brandis II and III do provide motivation to make them as they are specifically enumerated in the disclosure. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein

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sequences without affecting the function of the protein". The ordinary artisan would have had a reasonable expectation of success that the particular R and Q mutants would have possessed reduced discrimination given that 16 of 19 possible amino acid mutants made by Brandis II or III possessed this property and that other amino acids in the same group as Q and R, respectively, possessed this property in view of the teachings of Baker. The ordinary artisan would have been motivated to make the additional amino acid mutants Q and R taught by Brandis II or III for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis II or III. Not only would have been "obvious to try" to make and use the claimed mutants as Brandis II or III provides specific teaching and motivation to make such mutations in thermostable polymerases, but the prior art of both Brandis II or III and Baker provide for a reasonable expectation of success. The results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

7. Claims 32, 50-51, 90-91, and 98-99 are rejected under 35 USC 103(a) as being unpatentable over Brandis I, II, or III each in view Gelfand (US Patent 5,939,292) and Baker as evidenced by Cormier.

Brandis I, II, and III teach mutant DNA polymerases having at least one mutation at position 681 with respect to Taq DNA polymerase, wherein the mutant DNA polymerase has at least 2 fold reduced discrimination against the incorporation of a fluorescein type dye labeled

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nucleotide as compared to a naturally occurring DNA polymerase. Brandis I, II, and III teach kits comprising the mutant polymerase and a fluorescently labeled nucleotide dye, fluorescein type dyes, and nucleotides which are any naturally occurring nucleotides (encompasses dNTP and rNTP).

With regard to claims 32 and 50-51, Brandis I, II and III teach to provide mutant polymerases comprising other mutations in addition to the discrimination mutations such as those at position 681 of Taq polymerase, including mutants outside the discrimination regions (col. 10, lines 9-23, Table 2, cols 19-22). Brandis I, II and III teach mutations at position 615 of Taq polymerase (instant SEQ ID NOS 18). Brandis I, II or III do not specifically teach a polymerase comprising *both* a mutation at position 681 and a mutation at position 615, however Gelfand teaches to use modified DNA polymerases with enhanced efficiency for incorporating unconventional nucleotides, such as ribonucleotides, using a polymerase with a mutation at position 615, corresponding to Taq polymerase, in methods of DNA sequencing (see abstract, cols 2-3). Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide a mutant DNA polymerase with both a mutation at position 681 and 615, relative to Taq, both taught by Brandis, in the mutant polymerases of Brandis I, II or III for use in the sequencing methods or primer extension (minisequencing) methods taught by Brandis I, II or III because Gelfand teaches that the mutation at position 615 in a DNA polymerase provides for DNA polymerases that enable alternative nucleic acid synthesis methods for accurate and cost effective nucleic acid DNA sequence analysis. It would have further been prima facie obvious to the ordinary artisan at the time the invention was made to provide such mutant polymerases and a ribonucleotide labeled with a fluorescein type family

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dye for the purposes of making the methods of Brandis I, II or III, each in view of Gelfand more convenient to perform.

With regard to the various independent claims and dependent which recite that the amino acid at position 4 (exemplified by position 681 in Taq by Brandis) is Arg (R) or Gln (Q), Brandis does not teach actually making or testing these particular mutants, but do list the amino acids in Table 2. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein" (see col 10, lines 4-10). As evidenced by Cormier, standard conservative groups of amino acids include uncharged polar amino acid group which contains G, S, T, C N, Q and the basic amino acid group which contains K, R, and H. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed the particular R and Q mutants in the thermostable polymerase of Brandis and Gelfand and to have used such mutants as taught by Brandis in view of the teachings of Brandis and Baker. Brandis specifically teach that the basic amino acid K and H possessed reduced discrimination as did the polar uncharged amino acids S, C, N, T and that most of the mutants have 3 fold lower discrimination. Although Brandis does not teach having made the mutants, Brandis does provide motivation to make them as they are specifically enumerated in the disclosure. Further, Baker teaches that "It is well known in the biological arts that conservative amino acid substitutions can be made in protein sequences without affecting the function of the protein". The ordinary artisan would have had a reasonable expectation of success that the particular R and Q mutants would have possessed reduced discrimination given that 16 of 19 possible amino acid mutants made by Brandis possessed this property and that other amino acids in the same group as Q and

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R, respectively, possessed this property in view of the teachings of Baker. The ordinary artisan would have been motivated to make the additional amino acid mutants Q and R taught by Brandis for the purpose of providing a number of mutant polymerases with reduced discrimination against incorporation of a fluorescein type dye labeled nucleotide as taught by Brandis. Not only would have been “obvious to try” to make and use the claimed mutants as Brandis provides specific teaching and motivation to make such mutations in thermostable polymerases, but the prior art of both Brandis and Baker provide for a reasonable expectation of success. The results would have been predictable to one of ordinary skill in the art (see Examination Guidelines for Determining Obviousness Under 35 USC 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* Federal Register, Vol 72, No 195, October 2007).

Response to Arguments

8. The response traverses the rejections over Brandis and asserts that Brandis does not teach or suggest what effect, if any, mutation of position 4 to Q or R would have on the incorporation of fluorescein labeled nucleotides. The response points to col 8, lines 9-15 of the Brandis patent and asserts that the section does not teach or suggest that amino acids other than those listed can be substituted at position 681 but rather teaches away from the claimed invention because it omits Q and R but implies that the listing of possible substitutions is complete, suggesting that the listed substitutions are the only substitutions possible and implying that others are unsuitable. This argument has been thoroughly reviewed but was found unpersuasive. Taking into account the entire teaching of Brandeis, it appears that the omission of Q and R from the paragraph cited

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by applicant is not an implication that amino acids not listed are unsuitable, but rather appears to be a reflection of the results Brandeis reports. At table 2, under the heading "E681 Mutants", Brandeis lists all possible amino acid substitutions at position 681, but reports values for only the amino acids listed in the paragraph cited by applicant. Notably, both Q and R are listed, however it appears from the lack of a Tet Selectivity ratio or specific activity, that the Q and R mutants were not made or tested. Further, as seen from the table, all amino acids in the same family as Q and R, respectively have a ratio greater than 1, indicating improved incorporation of the fluorescently labeled nucleotide. As such, Brandeis not only appears to suggest the effect of Q and R on the discrimination properties of the mutant polymerase but given the teachings of Brandis and Baker, the effect of such mutants were predictable.

The response asserts that the Declaration of Dr. Gelfand (filed 1/3/2003) teaches that both Q and R generate improved discrimination over the wildtype *Thermus* "E", and that the substitution with R resulted in the best [reduced] discrimination which represent results that are superior and could not have been predicted from the cited art. The response asserts that this is surprising given that Brandis teaches that substitution with M was best. This argument has been thoroughly reviewed but was not found persuasive. It is noted that the type of nucleotide (dCTP vs ddCTP) as well as the label (Tet(II) vs HEX-2-PA used in Brandis and Dr. Gelfand's declaration are different and that Brandis teaches at col 6, lines 27-37 "The precise degree of discrimination will also vary in accordance with the specific fluorescently labeled nucleotide assayed, e.g. variations in base, dye, or linker. Mutant DNA polymerase of the invention may exhibit anywhere from a slight reduction in discrimination... to a complete elimination of discrimination". Accordingly, the ordinary artisan would have expected the exact levels of

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discrimination to differ based on base, dye or linker used in the assay. Further, although R showed the most reduced discrimination in Dr. Gelfand's declaration, such discrimination was on the same order of magnitude as a number of the same mutants which Brandis teaches showed reduced discrimination.

The response cites *Pfizer, Inc. v. Apotex, Inc.*, 82 USPQ2d 1321 (Fed. Cir. 2007) and asserts that there is no clear teaching what the "intended purpose" of the amino acid substitutions would be in contrast to the pharmaceutically acceptable salts at issue in the Pfizer case. This argument has been thoroughly reviewed but was not found persuasive for the reasons made of record above. Given the guidance in the prior art as noted above, the affect of the Q and R mutants would have been predictable to the ordinary artisan. It is further noted that the Court in *Pfizer* reiterated that the expectation of success be reasonable, not absolute. As in *Pfizer*, this is not a case where there are numerous parameters to try, rather the parameter that is varied is the amino acid and Brandis already made 16 of the 19 possible mutants and all functioned to provide reduced discrimination of fluorescently labeled dyes. Further, *as evidenced by the teachings of Brandis*, testing these mutants was routine at the time the invention was made.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

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Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 31 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13-16, 20-24, 27-32, 36-44 and 48-52 of copending Application No. 09/823,649, (now US Patent 7,179,590) and Giardano (US Patent 6,107,029).

Claim 31 is drawn to a method of producing labeled DNA by providing a mutant thermostable DNA polymerase comprising LSX[RQ]L[AS]IPXXE, a fluorescein family dye labeled nucleotide and performing a DNA synthesis reaction. The instant specification defines a "DNA synthesis reaction" to encompass PCR, SDA, transcription mediated amplification, primer extension, and reverse transcription.

The claims of the '649 application are directed to methods of reverse transcription using a mutant thermostable polymerase which comprises L[SA]X[-EAGPD][LI][SA]XXXXE and treating a reaction mixture to initiate synthesis of an extension product to provide a cDNA. The claims further limit the polymerase to a mutant thermostable polymerase such as *Thermus thermophilus*, which has an I at position 7 and a P at position 8 of instantly claimed SEQ ID NO: 1, as well as defining claimed polymerases in terms of additional polymerases such as *Thermus specie Z05* (see table 1). Accordingly, it is clear that the mutant polymerases in the instant claims and the claims of the '649 application are coextensive in scope. The claims differ in that the claims of the '649 application do not provide for a fluorescein family dye labeled nucleotide,

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however Giordano teaches that synthesizing labeled cDNA from an RNA molecule allows use of the cDNA to screen a library of genes thought to contain the gene encoding an RNA of interest (see col 10, lines 3-8). Additionally, Giordano teaches the use of labels such as fluorescein dyes (col. 7, lines 15-20). Therefore, it would have been prima facie obvious to one of one of ordinary skill in the art at the time the invention was made to modify the DNA synthesis reaction of '649 to label cDNA molecules as taught by Giordano. The ordinary artisan would have been motivated to produce labeled cDNA in the methods of '649 for the purpose of providing cDNA which could be used to screen a library of genes for an RNA of interest as taught by Giordano.

The response does not provide any arguments regarding the instant Obviousness type Double Patenting Rejection.

Conclusion

11. No claims are allowed.

12. It is noted that the filing of a declaration under 37 CFR 1.131 cannot be used to swear behind claims directed to subject matter which is claimed by the '193 patent. See MPEP 715 II:

An affidavit or declaration under 37 CFR 1.131 is not appropriate in the following situations:...

(B) Where the reference U.S. patent or U.S. patent application publication claims the same patentable invention. See MPEP § 715.05 for a discussion of "same patentable invention" and MPEP *> Chapter 2300<.

With regard to claims directed to subject matter claimed in a Publication for Patent, see MPEP 715.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-

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0752. The examiner can normally be reached Monday, Wednesday and Thursday from 9:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Acting Director of Technology Center 1600